

What is claimed is:

1. A method for isolation of a target comprising the steps of:  
dispersing one or more probe beads in a thixotropic agent;  
scanning for probe beads that generate a detectable signal from interaction between the one or more probe beads and the target; and  
5 picking one or more probe beads based on the detectable signal.
2. The method of claim 1, further comprising the step of extracting the target from the probe bead.
3. The method of claim 1, further comprising the step of identifying the target by mass spectrometry after liquid chromatography.
- 10 4. The method of claim 1, further comprising the step of identifying the target using mass spectrometry comprises matrix assisted laser desorption ionization mass spectrometry.
5. The method of claim 1, wherein the probe beads comprise an S-ODN library.
6. The method of claim 1, wherein the probe beads comprise an S<sub>2</sub>-ODN library.
7. The method of claim 1, wherein each of the probe beads are further modified to comprise a  
15 colorimetric agent.
8. The method of claim 1, wherein each of the probe beads further comprise one or more bases that are attached to a fluorophor.
9. The method of claim 1, wherein each of the probe beads further comprises one or more fluorophors attached to the 5' end, the 3' end or internally within the aptamers.
- 20 10. The method of claim 1, wherein a probe on the probe bead comprise an isolated and purified aptamer, a thioaptamer, a DNA, a RNA, a PNA, a peptide, an antibody, a cell, a cell fragment, a carbohydrate, a lipid and mixtures or combinations thereof.
11. The method of claim 1, wherein the probe beads comprise an aptamer and the aptamer is defined further as comprising a thioaptamer.
- 25 12. The method of claim 1, wherein the probe beads comprise an aptamer are defined further as comprising a thioaptamer and wherein one or more but less than all of the linkages comprising one or more of the following: rATP(αS), rUTP(αS), rGTP(αS), rCTP(αS), rATP(αS<sub>2</sub>), rUTP(αS<sub>2</sub>), rGTP(αS<sub>2</sub>), rCTP(αS<sub>2</sub>), rATP(αS), dTTP(αS), dGTP(αS), dCTP(αS), dATP(αS<sub>2</sub>), dTTP(αS<sub>2</sub>), dGTP(αS<sub>2</sub>) and dCTP(αS<sub>2</sub>).
- 30 13. The method of claim 1, wherein the target is labeled with an enzyme, a dye, a radioisotope, an electron dense particle, a magnetic particle, a fluorescent agent, an antibody, a magnetic particle or a chromophore.

14. The method of claim 1, wherein the target is detectable with an enzyme, a radioisotope, an electron dense particle, a magnetic particle, a fluorescent agent, an antibody, a magnetic particle or a chromophore.
15. The method of claim 1, wherein the probe bead is further processed to remove the target bound to the aptamer bead.  
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16. The method of claim 1, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ.
17. The method of claim 1, probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ by proteolysis and transferred to the inlet of an LC-MS or an  
10 LC-MS/MS.
18. The method of claim 1, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for MALDI-MS analysis, wherein the MALDI-MS analysis is selected from the group consisting of MALDI-TOF/MS, MALDI-TOF/TOF-MS and MALDI-Q-TOF-MS.
19. The method of claim 1, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for LC-MS analysis.  
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20. The method of claim 1, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for MALDI-MS analysis.
21. The method of claim 1, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for MALDI-MS analysis by SELDI ionization.  
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22. The method of claim 1, wherein the probe bead is further processed to remove the target bound to the aptamer bead and analyzing the target by MS, MS/MS, MALDI-TOF, MALDI-TOF-MS, direct sequencing.
23. The method of claim 22, wherein the MALDI ionization step is a SELDI ionization.  
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24. The method of claim 1, wherein the probe bead is further processed to remove the target bound to the aptamer bead and analyzing the target by binding a second detectable label to the target.
25. The method of claim 1, wherein the thixotropic agent comprises a polyacrylamide gel, an alkyd resin or a silica-lipid.
26. The method of claim 1, wherein picking the one or more probes beads is selected from picking manually, semi-manually or non-manually.  
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27. The method of claim 1, wherein the target is selected from peptides, proteins, nucleic acids, carbohydrates, lipids or combinations thereof.
28. The method of claim 1, wherein the one or more probe beads are dispersed within the thixotropic agent by molecular printing.

29. The method of claim 1, wherein the one or more probe beads are dispersed within the thixotropic agent using an ink-jet printer.
30. A method for aptamer selection comprising the steps of:
  - dispersing a one-aptamer, one-bead combinatorial bead library into a two-dimensional matrix;
  - scanning for aptamer beads that generate a detectable signal from interaction between the one or more aptamer beads and a target; and
  - picking one or more aptamer beads based on the detectable signal from within the matrix.
31. The method of claim 30, further comprising the step of extracting the target from the aptamer bead.
- 10 32. The method of claim 30, further comprising the step of identifying the target by mass spectrometry after liquid chromatography.
33. The method of claim 30, wherein the one-aptamer, one-bead combinatorial bead library is dispersed within the matrix by molecular printing.
- 15 34. The method of claim 30, wherein the one-aptamer, one-bead combinatorial bead library is dispersed within the matrix by molecular printing is via an inkjet printer.
35. The method of claim 30, wherein the matrix comprises a gel, a polymer, a thixotropic agent, a glass or a silicon matrix.
36. The method of claim 30, further comprising the step of separating the target into one or more peptides prior to separation by liquid chromatography.
- 20 37. The method of claim 30, wherein the steps of identifying the target by mass spectrometry is preceded by the steps of extracting and separating the proteins by liquid chromatography.
38. The method of claim 30, wherein the steps of identifying the target using mass spectrometry comprises matrix assisted laser desorption ionization (MALDI) mass spectrometry.
39. The method of claim 30, wherein the library comprises an S-ODN library.
- 25 40. The method of claim 30, wherein the library comprises an S<sub>2</sub>-ODN library.
41. The method of claim 30, wherein each of the aptamers is further modified to comprise a colorimetric agent.
42. The method of claim 30, wherein each of the aptamers further comprises one or more bases that are attached to a fluorophor.
- 30 43. The method of claim 30, wherein each of the aptamers further comprises one or more fluorophors attached to the 5' end, the 3' end or internally within the aptamers.
44. The method of claim 30, further comprising the complementary strand to the aptamer.
45. The method of claim 30, wherein the aptamer is defined further as a thioaptamer.

46. The method of claim 30, wherein the aptamer comprises a thioaptamer wherein one or more but less than all of the linkages comprising one or more of the following: rATP(αS), rUTP(αS), rGTP(αS), rCTP(αS), rATP(αS<sub>2</sub>), rUTP(αS<sub>2</sub>), rGTP(αS<sub>2</sub>), rCTP(αS<sub>2</sub>), rATP(αS), dTTP(αS), dGTP(αS), dCTP(αS), dATP(αS<sub>2</sub>), dTTP(αS<sub>2</sub>), dGTP(αS<sub>2</sub>) and dCTP(αS<sub>2</sub>).
- 5 47. The method of claim 30, wherein the target is labeled with an enzyme, a dye, a radioisotope, an electron dense particle, a magnetic particle, a fluorescent agent, an antibody, a magnetic particle or a chromophore.
48. The method of claim 30, wherein the target is detectable with an enzyme, a radioisotope, an electron dense particle, a magnetic particle, a fluorescent agent, an antibody, a magnetic particle or a  
10 chromophore.
49. The method of claim 30, wherein the aptamer bead is further processed to remove the target bound to the aptamer bead.
50. The method of claim 30, wherein the aptamer bead is acquired by a scanning robotic head and the target is extracted from the aptamer bead in situ.
- 15 51. The method of claim 30, aptamer bead is acquired by a scanning robotic head and the target is extracted from the aptamer bead in situ by proteolysis and transferred to the inlet of an LC-MS or an LC-MS/MS.
52. The method of claim 30, wherein the aptamer bead is acquired by a scanning robotic head and the target is extracted from the aptamer bead in situ for MALDI-MS analysis, wherein the  
20 MALDI-MS analysis is selected from the group consisting of MALDI-TOF/MS, MALDI-TOF/TOF-MS and MALDI-Q-TOF-MS.
53. The method of claim 30, wherein the aptamer bead is acquired by a scanning robotic head and the target is extracted from the aptamer bead in situ for LC-MS analysis.
54. The method of claim 30, wherein the aptamer bead is acquired by a scanning robotic head  
25 and the target is extracted from the aptamer bead in situ for MALDI-MS analysis.
55. The method of claim 30, wherein the aptamer bead is acquired by a scanning robotic head and the target is extracted from the aptamer bead in situ for MALDI-MS analysis by SELDI ionization.
56. The method of claim 30, wherein the aptamer bead is further processed to remove the target  
30 bound to the aptamer bead and analyzing the target by MS, MS/MS, MALDI-TOF, MALDI-TOF-MS, direct sequencing.
57. The method of claim 56, wherein the MALDI ionization step is a SELDI ionization.
58. The method of claim 30, wherein the aptamer bead is further processed to remove the target bound to the aptamer bead and analyzing the target by binding a second detectable label to the target.

59. The method of claim 30, wherein the matrix comprises a polyacrylamide gel, an alkyd resin or a silica-lipid.
60. The method of claim 30, wherein picking the beads is selected from picking manually, semi-manually or non-manually.
- 5 61. The method of claim 30, wherein the target is selected from peptides, proteins, nucleic acids, carbohydrates, lipids or combinations thereof.
62. A system for target identification comprising:  
a two-dimensional matrix for separation of two or more probe beads bound to a target;  
a scanner that images a signal from the two or more probe beads bound to a target; and  
10 a spot-picker that picks one or more probe beads bound to a target.
63. The system of claim 62, wherein the spot-picker transfers one or more probe beads bound to a target to a chamber for further chemical manipulation.
64. The system of claim 62, wherein the spot-picker transfers one or more probe beads bound to a target to a chamber for probe sequencing.
- 15 65. The system of claim 62, wherein the spot-picker transfers one or more probe beads bound to a target to a chamber for target identification.
66. The system of claim 62, wherein the spot-picker comprises a robotic spot picker.
67. The system of claim 62, wherein the two-dimensional matrix comprises a gel, a polymer, a thixotropic agent, a glass or a silicon matrix.
- 20 68. The system of claim 62, wherein the spot-picker transfers one or more probe beads bound targets to a probe bead-target separator; and  
a conduit to transfer separated targets into a liquid chromatograph.
69. The system of claim 62, wherein the spot-picker transfers one or more probe beads bound targets to a bead-target separator; and  
25 one or more conduits connected to the bead-target separator to transfer separated targets to a liquid chromatograph and a mass spectrometer.
70. The system of claim 62, wherein the spot-picker transfers one or more probe beads bound targets to a probe bead-target separator; and  
one or more conduits connected to the probe bead-target separator to transfer separated targets to a  
30 liquid chromatograph and a mass spectrometer, therein the mass spectrometer comprising a MALDI-MS.
71. The system of claim 62, wherein the probe beads comprise an aptamer are defined further as comprising a thioaptamer and wherein one or more but less than all of the linkages comprising one or more of the following: rATP( $\alpha$ S), rUTP( $\alpha$ S), rGTP( $\alpha$ S), rCTP( $\alpha$ S), rATP( $\alpha$ S<sub>2</sub>), rUTP( $\alpha$ S<sub>2</sub>),

rGTP(αS<sub>2</sub>), rCTP(αS<sub>2</sub>), rATP(αS), dTTP(αS), dGTP(αS), dCTP(αS), dATP(αS<sub>2</sub>), dTTP(αS<sub>2</sub>), dGTP(αS<sub>2</sub>) and dCTP(αS<sub>2</sub>).

72. The system of claim 62, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ.

5 73. The system of claim 62, probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ by proteolysis and transferred to the inlet of an LC-MS or an LC-MS/MS.

10 74. The system of claim 62, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for MALDI-MS analysis, wherein the MALDI-MS analysis is selected from the group consisting of MALDI-TOF/MS, MALDI-TOF/TOF-MS and MALDI-Q-TOF-MS.

75. The system of claim 62, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for LC-MS analysis.

15 76. The system of claim 62, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for MALDI-MS analysis.

77. The system of claim 62, wherein the probe bead is acquired by a scanning robotic head and the target is extracted from the probe bead in situ for MALDI-MS analysis by SELDI ionization.

78. The system of claim 62, wherein the probe bead is further processed to remove the target bound to the aptamer bead and analyzing the target by MS, MS/MS, MALDI-TOF, MALDI-TOF-20 MS, direct sequencing.

79. The system of claim 62, wherein the MALDI ionization step is a SELDI ionization.

80. The system of claim 62, wherein a probe on the probe bead comprise an isolated and purified aptamer, a thioaptamer, a DNA, a RNA, a PNA, a peptide, an antibody, a cell, a cell fragment, a carbohydrate, a lipid and mixtures or combinations thereof.

25 81. A system for aptamer selection comprising:

a two-dimensional matrix for separation of two or more aptamer beads bound to a target;  
a scanner that images a signal from the two or more aptamer beads bound to a target; and  
a spot-picker that picks one or more aptamer beads bound to a target.